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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
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EXAMINER	
NOGUEROLA, A	
ART UNIT	**PAPER NUMBER**
1743	3

DATE MAILED: 06/25/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/044,350	John Peeters
Examiner	**Group Art Unit**
Alex Noguerola	1744

☒ Responsive to communication(s) filed on *Mar 19, 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-37* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *19-21* is/are allowed.

☒ Claim(s) *1-18, 22-26, and 29-37* is/are rejected.

☒ Claim(s) *27 and 28* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413.

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claim 2-4, 6-13, 15, 17, and 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that dependent claims will have the deficiencies of base and intervening claims.

a) claim 2: while it may be ultimately true that one is many and many are one, one electrode is not many electrodes;

b) claim 9, line 2: "height" is indefinite. Does "height" mean length or distance above an analyte, or something else?

c) claim 31 is a method claim yet it depends from claim 2, an apparatus claim;

d) claim 32, line 2: "Angstrom level precision" is indefinite. Is the silicon chip or the sensor on the order of several Angstroms?

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. Claims 32-35 are rejected under 35 U.S.C. 102(e) as being clearly anticipated in the case of claims 32-34 and anticipated in the case of claim 35 by Lipskier (US 5,910,286).

Addressing claim 32. See the abstract; column 5, lines 14-16 and col. 6, ln. 17-21.

Addressing claims 33 and 34. See Figure 3 and col. 5, ln. 14-19.

Addressing claim 35. A protein-specific receptor is anticipated is anticipated because Lipsker teaches a polypeptide-specific receptor (col. 6, lines 17-21).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-13, 16-18, 25, 26, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagawa (US 5,730,940) in view of WPIDS abstract of Zhang et al. (CN 11107896).

Addressing claim 1. Nakagawa teaches a sensor for detecting biological molecules, the sensor comprising

a substrate; and

an electrode having the capacity to bind a preselected biological molecule. See the abstract; Fig. 3, 5(a), 5(b), and 6; column 7, lines 32-35; and col. 8, ln. 27-35. Nakagawa does not mention that the electrode dimensions, specifically that the electrode is between about 10^{-9} and 10^{-10} meters in height or width, although he does disclose for the atomic force microscope embodiment "base diameter of about 4 μm, length about 1 μm, curvature - radius of the tip about 0.5 to 1 μm ... These dimensions, however, are not specifically limited" (col. 8, ln. 22-60). Additionally, Nakagawa is concerned with scanning the sample with an "atomic level of precision" (col. 8, ln. 39) which strongly suggests very small dimensions. In fact "[t]he scanning area of the probe was 100 x 100 nm^2 (col. 21, ln. 13-16).

Zhang et al. teach an electrode "with minimal size of 30 nm. The electrode features controllable size, molecule-class surface smoothness and high mechanical strength, so it may be used for measuring a single cell" (the abstract). It would have been obvious to one with ordinary skill in

the art at the time the invention was made to have the electrode on the order of 10^{-9} meters as taught by Zhang et al. in the invention of Nakagawa because a smaller electrode will allow molecules to be detected that are in confined regions, such as a channel, rather than on a relatively flat surface (Fig. 6 in Nakagawa, for example). A change in size has been held obvious. In re Rose, 105 USPQ 237.

Addressing claims 2-4. Nakagawa does not mention multiple electrodes in the sensor. It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide multiple electrodes in order to detect different molecules or atoms, for example, one electrode for detecting cytosine and another electrode from guanine. Alternatively, additional electrodes could be provided so that a particular molecule or atom would be detected over a wider region in a shorter amount of time than just one electrode scanning alone. See in Nakagawa col. 10, ln. 8-38 and col. 21, ln. 44-54. Duplication of parts was held to have been obvious. In re Harza 124 USPQ 378.

Addressing claims 5 and 6. See in Nakagawa Fig. 5(a) and col. 7, ln. 32-35.

Addressing claim 7. The same coating would be provided so that a particular molecule or atom could be detected over a wider region in a shorter amount of time than just one electrode scanning alone.

Addressing claim 8. Different coatings would be provided in order to allow detection of different molecules or atoms, for example, one coating for detecting cytosine and another coating for guanine.

Addressing claims 9-12, 17. Nakagawa does not mention the claimed references; however, it would have been obvious to one with ordinary skill in the art at the time the invention was made to have the dimensions and spacings, or clustering of the electrodes arranged so as to most efficiently scan the surface containing the analyte to e detected.

Addressing claim 13. See in Nakagawa Fig. 6 and col. 7, ln. 32-35.

Addressing claim 16. See in Nakagawa Fig. 2 and col. 7, ln. 52-64.

Addressing claim 18. See in Nakagawa col. 17, ln. 39-54.

Addressing claim 25. Nakagawa teaches a method of sequencing nucleic acids, comprising all of applicant's claimed limitations except for a plurality of electrodes and that the electrodes are

between about 10^{-9} and 10^{-10} meters in height or width. See the abstract; Fig. 3, 5(a), 5(b), and 6; column 7, lines 32-35; col. 8, ln. 27-35.

As for a plurality of electrodes, it would have been obvious to one with ordinary skill in the art at the time the invention was made to provide multiple electrodes in order to detect different molecules or atoms, for example, one electrode for detecting cytosine and another electrode from guanine. Alternatively, additional electrodes could be provided so that a particular molecule or atom would be detected over a wider region in a shorter amount of time than just one electrode scanning alone. See in Nakagawa col. 10, ln. 8-38 and col. 21, ln. 44-54. Duplication of parts was held to have been obvious. In re Harza 124 USPQ 378.

As for the claimed electrode dimensions, although Nakagawa does not mention the claimed electrode dimensions, he does disclose for the atomic force microscope embodiment "base diameter of about 4 μm, length about 1 μm, curvature - radius of the tip about 0.5 to 1 μm ... These dimensions, however, are not specifically limited" (col. 8, ln. 22-60). Additionally, Nakagawa is concerned with scanning the sample with an "atomic level of precision" (col. 8, ln. 39) which strongly suggests very small dimensions. In fact "[t]he scanning area of the probe was 100 x 100 nm^2 (col. 21, ln. 13-16).

Zhang et al. teach an electrode "with minimal size of 30 nm. The electrode features controllable size, molecule-class surface smoothness and high mechanical strength, so it may be used for measuring a single cell" (the abstract). It would have been obvious to one with ordinary skill in the art at the time the invention was made to have the electrode on the order of 10^{-9} meters as taught

by Zhang et al. in the invention of Nakagawa because a smaller electrode will allow molecules to be detected that are in confined regions, such as a channel, rather than on a relatively flat surface (Fig. 6 in Nakagawa, for example). A change in size has been held obvious. In re Rose, 105 USPQ 237.

Additionally, although no direct mention is made of the electrodes binding nucleic acids, Nakagawa only discloses examples of the atomic force microscope interacting with nucleic acids, it is clear that the electrodes are also intended to be used on nucleic acids (col. 4, ln. 25-67).

Addressing claim 26. Nakagawa teaches complementary binding to different base pairs (col. 9, ln. 66 - col. 10, ln. 40).

Addressing claim 29. See in Nakagawa Fig. 3 and col. 8, ln. 27-60.

Addressing claim 30. See in Nakagawa col. 5, ln. 8-12.

Addressing claim 31. Assuming claim 31 depends from claim 25, although Nakagawa does not teach providing the claimed support strucuture, he does teach that spectroscopy analyzes the types of bonds (col. 1, ln.28-31). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide the claimed support structure becasue a fluorescent laser reader, that is spectroscopy, will provide complementary information to the structural information provided by the electrodes.

6. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagawa (US 5,730,940) in view of WPIDS abstract of Zhang et al. (CN 11107896) as applied to claims 1-13, 16-18, 25, 26, 29, 30 above, and further in view of CAPLUS abstract of Costa-Kramer et al. ("Metallic nanowires: conductance statistics, stability, IV curves, and magnetism", NATO ASI Ser. E (1997), 340(Nanowires), 171-190). Zhang et al. do not mention the dimension of the wire connected to the electrode. Costa-Kramer et al. teach properties of nanowires (abstract), in particular that each wire has a unique IV curve. Given that the electrodes in Zhang et al. are nanoscale it would have been obvious to one with ordinary skill in the art at the time the invention was made to connect nanoscale leads or wires to the electrodes in order to reduce distortion of the detection signal by using wire that is electrically compatible with the electrode.

7. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAPIO abstract of Hajme et al. in view of Nakagawa (US 5,730,940).

Addressing claim 22. Hajme et al. teaches all of applicant's limitations except for the cantilever being a micro cantilever; the abstract is silent on the dimensions of the cantilever. See the abstract. Nakagawa teaches a probe on a micro cantilever (abstract; col. 7, ln. 3-9 col. 8, ln. 21-26). It would have been obvious to one with ordinary skill in the art at the time the invention was made to scale the cantilever as taught by Nakagawa in the invention of Hajme et al. so that the sensor will detect at the desired level of precision, for example at the individual molecule or cell level, or at micromole level. A change in size has been held obvious. In re Rose, 105 USPQ 237.

Addressing claim 23. The details of the invention of Hajme et al. is not known to the Examiner as a translation is not currently available. Nakagawa teaches using laser light as a detection signal (col. 7, ln. 3-16).

Addressing claim 24. Nakagawa also teaches piezoelectric detector (col. 7, ln. 3-31).

8. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lipskier (US 5,910,286) as applied to claims 32-35 above, and further in view of David Page ("Principles of Biological Chemistry", Willard Grant Press, 1976, page 45). Lipskier does not mention deriving information from x-ray diffraction studies to make the sensor. Page teaches that x-ray crystallography is used for structure analysis of proteins (page 45). It would have been obvious to one with ordinary skill in the art at the time the invention was made to use information derived from x-ray diffraction to make the sensor because such information will provide important detail that will assist in the accurate design of the surface of the sensor.

9. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lipskier (US 5,910,286) as applied to claims 32-35 above, and further in view of CAPLUS abstract of Clowes et al. ("Improved methods for structural studies of proteins using nuclear magnetic resonance spectroscopy", Curr. Opin. Biotechnol. (1995), 6(1), 81-8). Lipskier does not mention deriving information from x-ray diffraction studies to make the sensor. Clowes et al. teach that NMR is used

for structure analysis of proteins (abstract). It would have been obvious to one with ordinary skill in the art at the time the invention was made to use information derived from NMR to make the sensor because such information will provide important detail that will assist in the accurate design of the surface of the sensor.

Allowable Subject Matter

10. Claims 19-21 are allowed.

11. Claims 27 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The following is a statement of reasons for the indication of allowable subject matter: Applicant's invention of a sensor for detecting proteins and a method of sequencing nucleic acids is an unobvious improvement over er the prior art of record.

The unobvious improvement in independent claim 19 is the combination of limitations requires that the electrodes with the specified dimension are disposed in the micro-capillary tube. Claims 20 and 21 depend directly or indirectly from claim 19.

The unobvious improvement in claim 27 is that the combination of limitations requires that the electrodes are disposed in a microtube. Claims 28 depends form claim 27.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alex Noguerola whose telephone number is (703)-305-5686.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Warden, can be reached at (703)-308-2920. The unofficial fax phone number, for example, for faxing a proposed amendment, for this Group is (703)-305-7719. The official fax phone number, for example, for faxing an amendment to be entered, for this Group is (703)-305-7718.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)-308-0651.

Alex Noguerola

June 21, 1999

T. TUNG
PRIMARY PATENT EXAMINER
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